## PSEUDO-RELAPSES IN CASES OF MALARIAL FEVER DURING CONTINUOUS QUININE TREAT-MENT

BY

SIR RONALD ROSS, K.C.B., F.R.S.,

AND

DAVID THOMSON, M.B., CH.B., D.P.H.

(Received for publication 18 September, 1911)

There seems to be a current belief that relapses may occasionally occur in cases of malarial fever even during continuous quinine treatment. Caccini (quoted by Ross, 1910) states that a relapse occurred in 15 per cent. of 1,002 cases which had quinine daily. We cannot, however, find accurate data regarding all these relapses, as to whether parasites were found in the blood during the relapse, or how much quinine had been given, or for what period. Again, from various sources it has been stated that cases of malaria occur in the Amazon region which are resistant to quinine treatment; but so far as we know accurate data are not given regarding the presence or absence of parasites during this unsuccessful treatment.

During the past two years we have been studying the effects of quinine on malaria, employing enumerative methods by which we constantly know the number of parasites present in the blood per c.mm. Seventy-five cases studied in this way all showed the remarkable destructive power of quinine towards the asexual malarial parasites. In all cases where quinine was given in doses of ten grains thrice daily, it was almost impossible to find asexual parasites in the blood after three days of the treatment, no matter how numerous the parasites were before the treatment was commenced. In no case did we ever discover a reappearance of these parasites while this dosage was continued.\* It would appear to us, that so far, no drug has been found with so great a curative

<sup>\*</sup> Such a case has, however, occurred while this article was in the press. It will be reported later.

power in any disease, as that of quinine in malaria. In our cases of malaria, which came from various parts of the world, including the Amazon, it never failed to show a very remarkable and rapid curative power. It is vastly superior to arsenic, methylene blue, trypan blue, picric acid, etc. We would like, however, to call attention to apparent relapses occurring during quinine treatment. In five (three cases P. falciparum, two cases P. vivax) or 6.7 per cent. of our cases, a sudden isolated rise of temperature occurred during the quinine treatment, accompanied sometimes with a feeling of cold and slight shivering. No asexual parasites could be detected on prolonged search by thick film during these attacks of fever. On one occasion the blood was examined by one of us and thirteen students for over half an hour, yet no parasites either sexual or asexual could be found. All these apparent relapses were, therefore, One naturally wonders if these are non-parasitic relapses. connected in any way with the malarial infection, or if it is due to the quinine treatment, or if they are mere coincidences, the fever being due to some other cause. We investigated the hospital records of one hundred cases of various diseases, not malarial, and found that similar more or less inexplicable isolated rises of temperature occurred in 17 per cent. of them. The diseases in which these isolated temperature rises occurred most frequently were cases of latent phthisis, cases of valvular heart disease, Bright's disease, chorea, rheumatism and bronchitis, and to a less frequent extent in various other conditions, and in one case of spastic paraplegia. These isolated and more or less inexplicable rises of temperature, therefore, occur in other diseases during treatment as well as in malaria, and it seems possible that they may have no real connection with the original disease. In some cases the temperature could be explained by a sudden and transitory inflammation of the tonsils. One of our cases of malaria had a slight tonsillitis during his pseudo-relapse. Again these rises of temperature in two of our cases did not occur on the proper day, so that they would appear not to be malarial.

Although numerous non-parasitic rises of temperature with rigors occur in blackwater fever, and although it has been shown by one of us (D. T.) that, from the behaviour of the leucocytes, one might infer that the malarial virus lingers long in the system in spite of

continuous quinine treatment, yet we have no proof that these pseudo-relapses are due to the disease. Some of the relapses during quinine treatment recorded by Caccini may possibly correspond to the 17 per cent. of incidental rises of temperature found in cases not malarial, during treatment in hospital. We therefore think that accurate enumerative observations are needed before the possibility of such relapses, and of cases resistant to quinine, can be fully accepted.

## LITERATURE

CACCINI (1902). 'Journ. of Tropical Medicine, Nos. 8, 9, 10, 11, 12.
Ross (1910'. Prevention of Malaria, p. 138.

Pseudo-Relapses During Quinine Treatment. (Three Cases. P. falciharum) Date J. M. Age 20 (P. fale.). 40° 340 38' 37 36° Date.
F.F. age 22.
(P. Felerharum) 40° 39° 380 36° d.c. Age 14 (P. falc.) Temperature (Cent.) Nog Asexval Parasites Arr Cham 10,000 39° 380

( D. Thomson. Del.)